

FDA Summary and Discussion Topics

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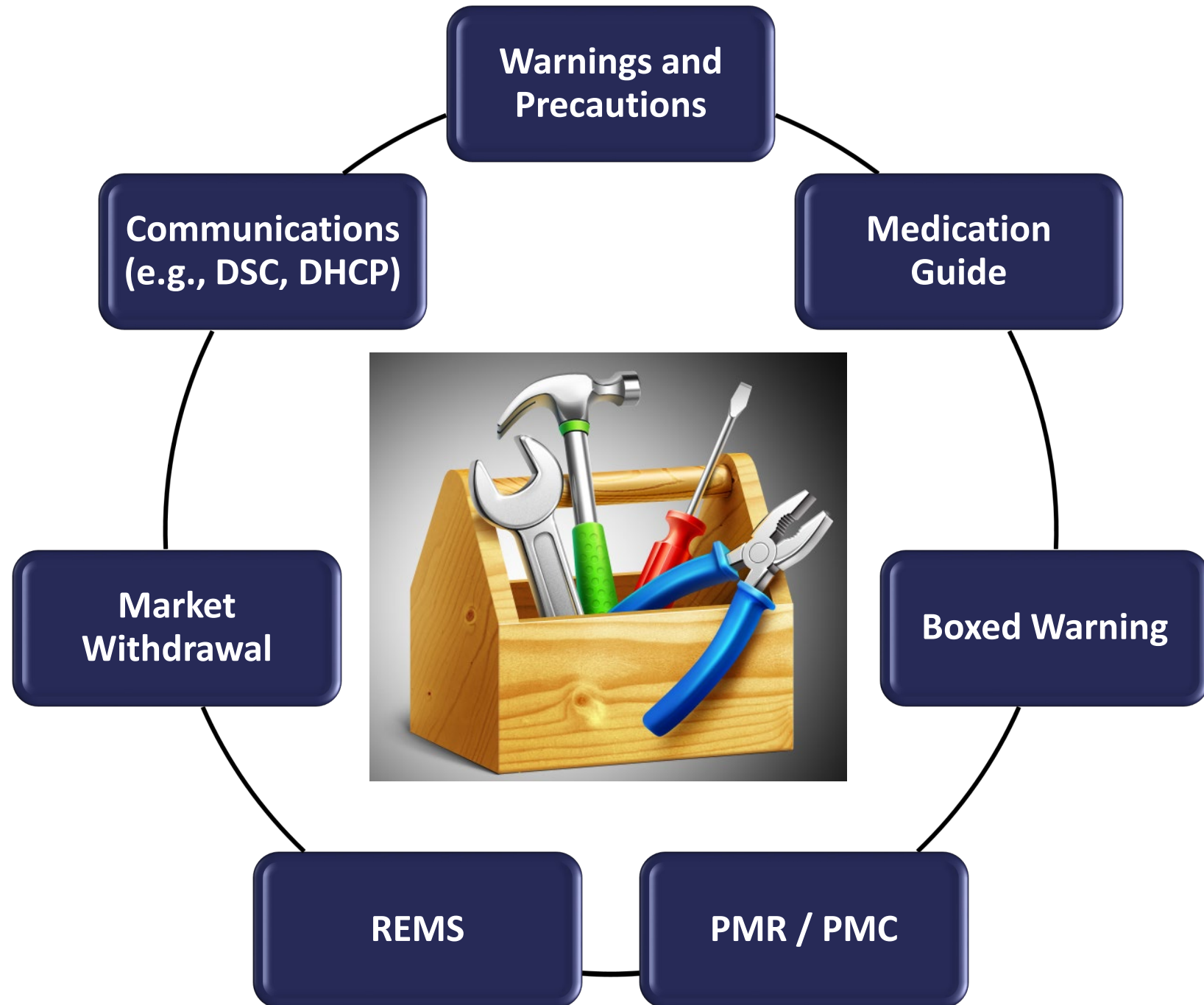
Summary

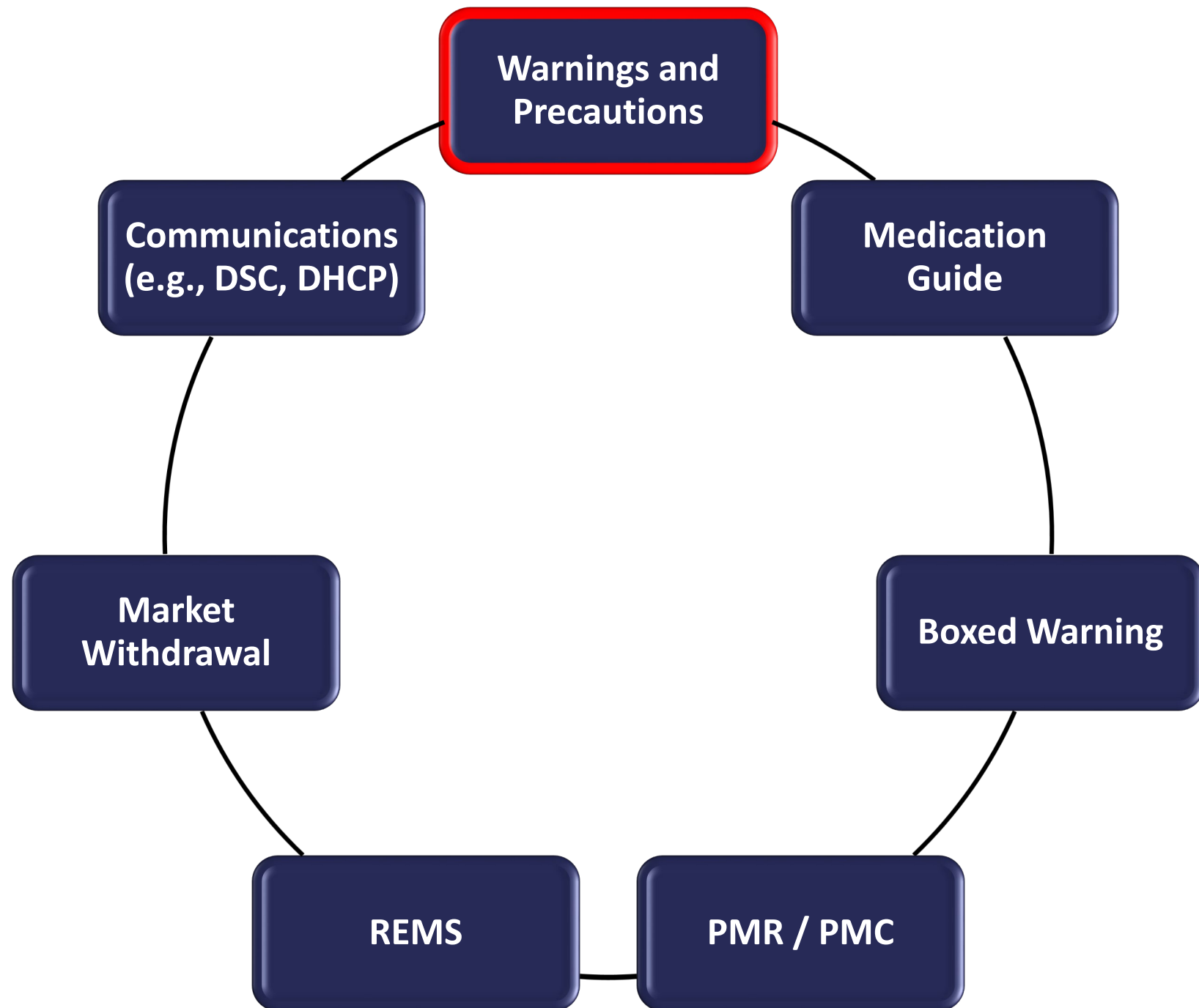
- Long-standing safety issue with montelukast and neuropsychiatric events
- Absence of strong safety signal in clinical trials for allergic rhinitis and asthma
- FAERS postmarketing reports
 - Wide range of events
 - Sparse information regarding withdrawal
 - Limitations
- Literature review
 - Mixed results from observational studies

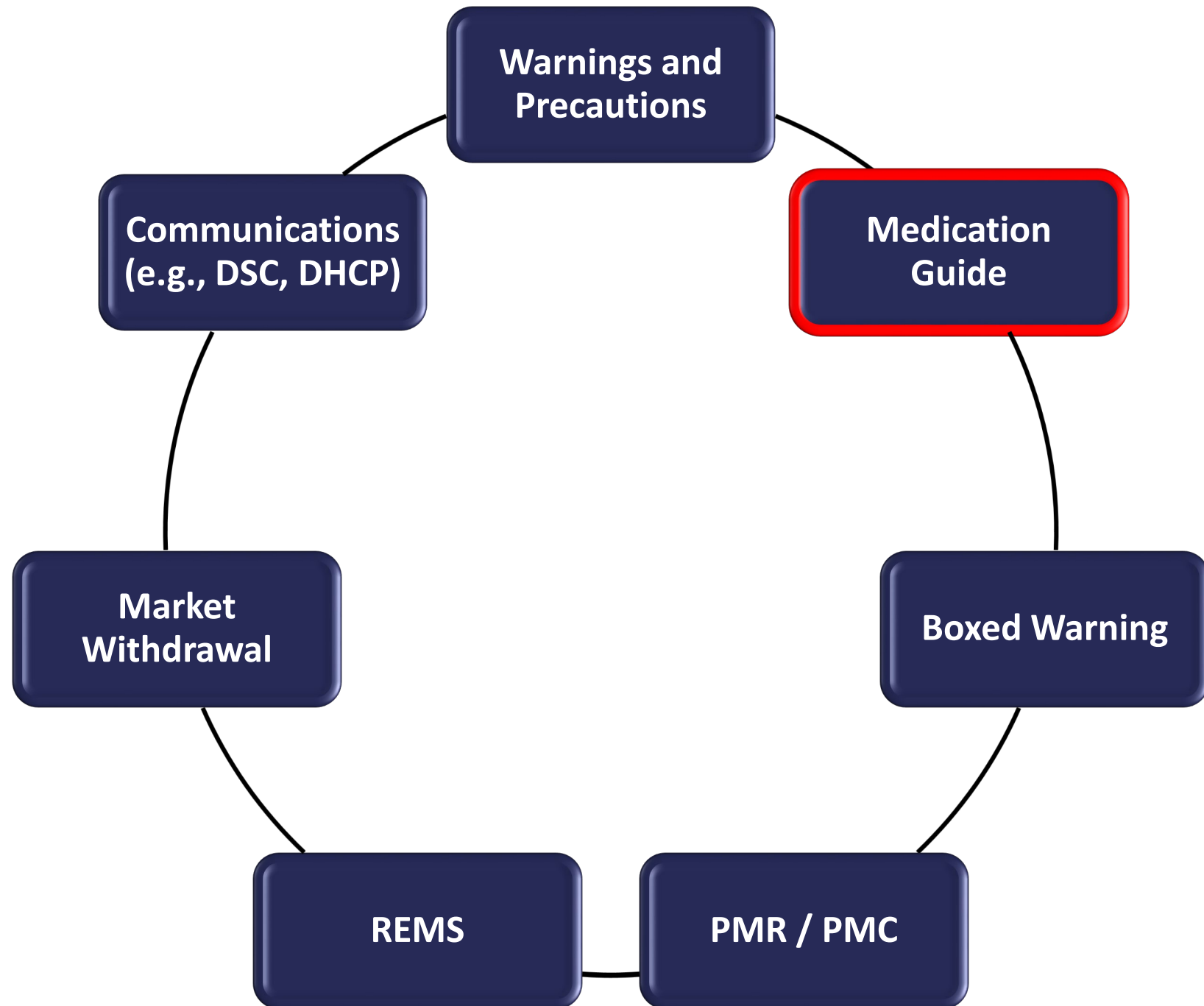
Summary

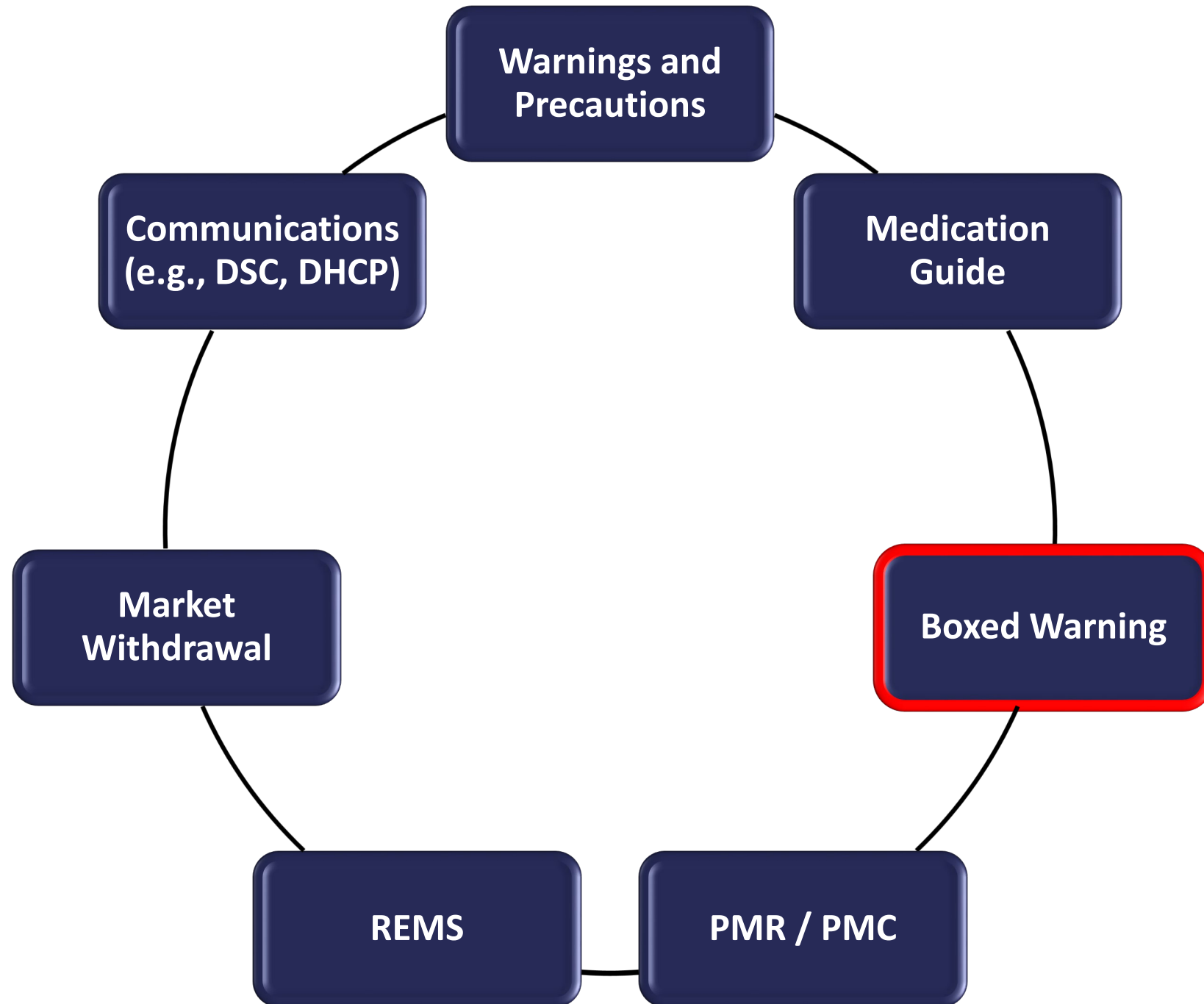
- Sentinel study
 - No statistical association with montelukast use and neuropsychiatric events of inpatient depressive disorder and self-harm
 - Death due to suicide was rare and limited to adults with a prior psychiatric history
- Communication is a challenge
 - Existing safety issue
 - Available data have limitations and/or inconclusive

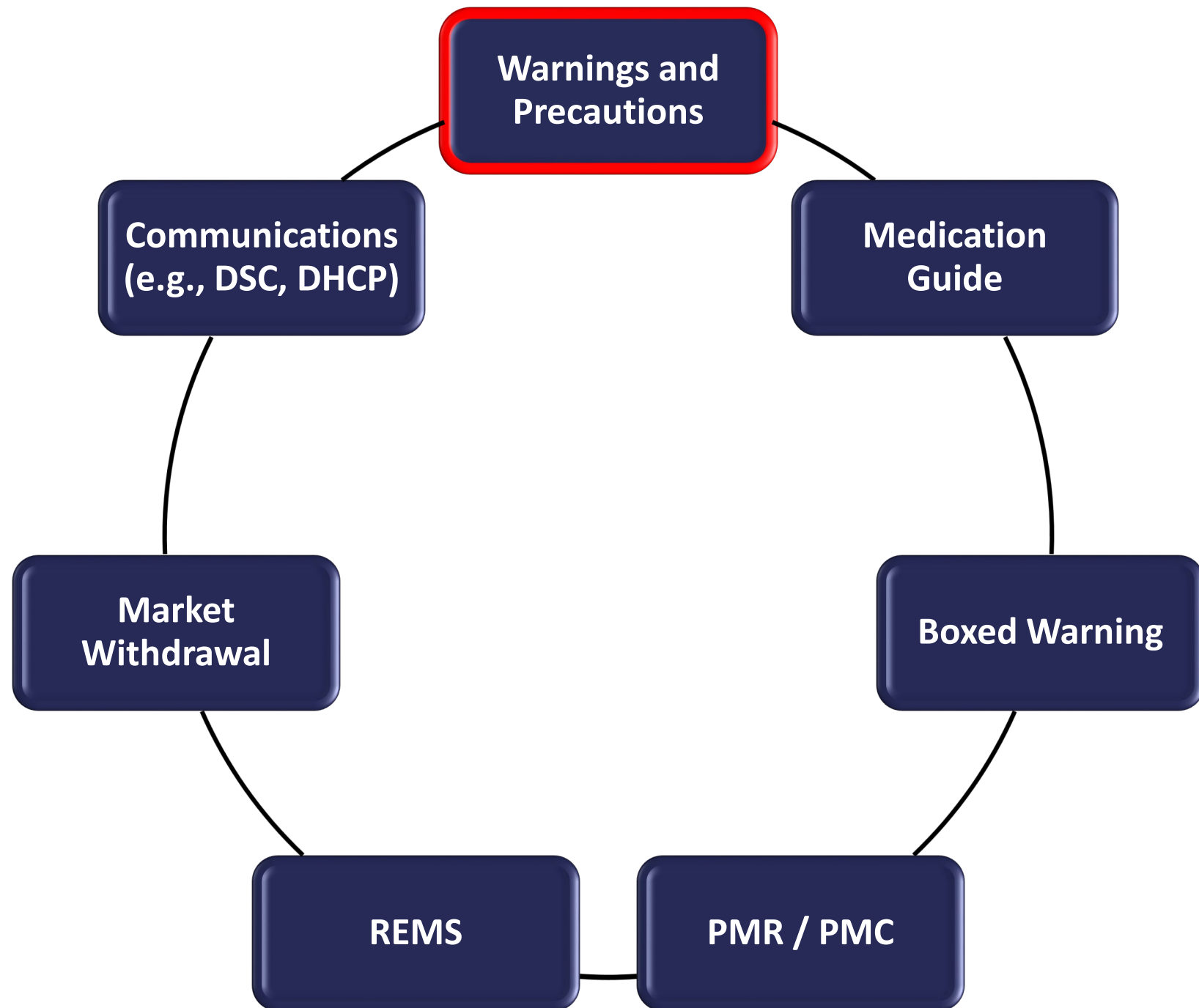
Regulatory considerations

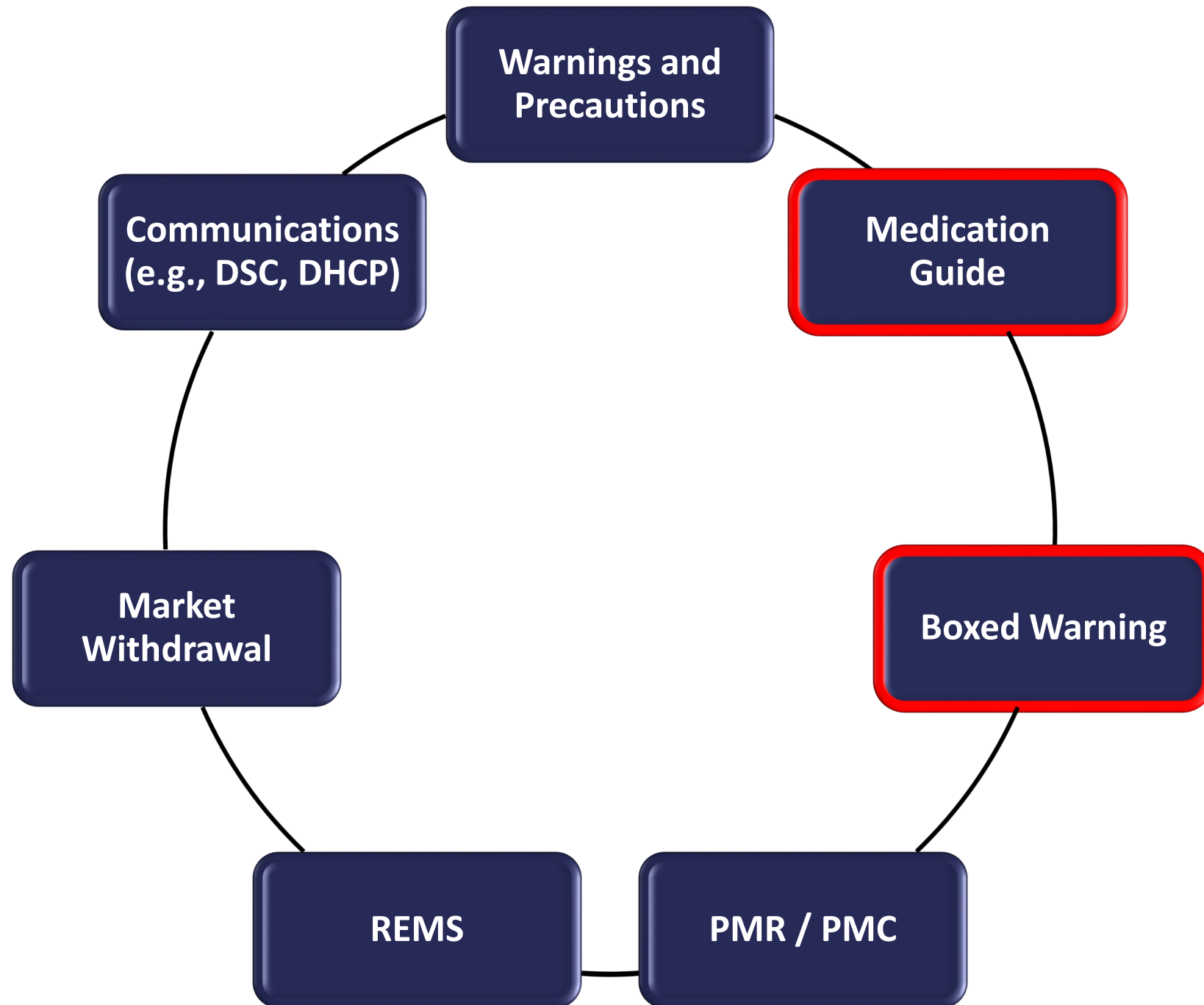


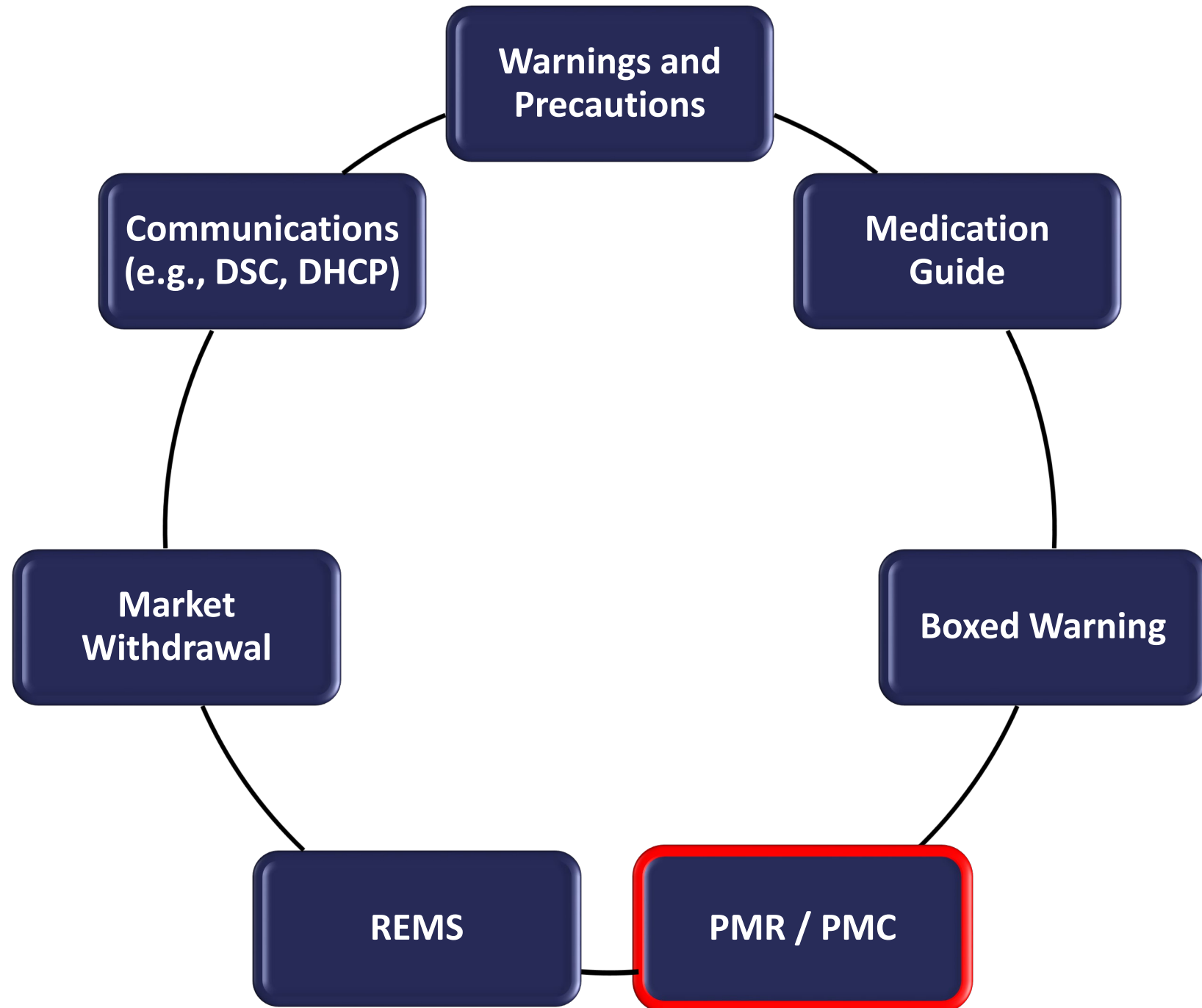


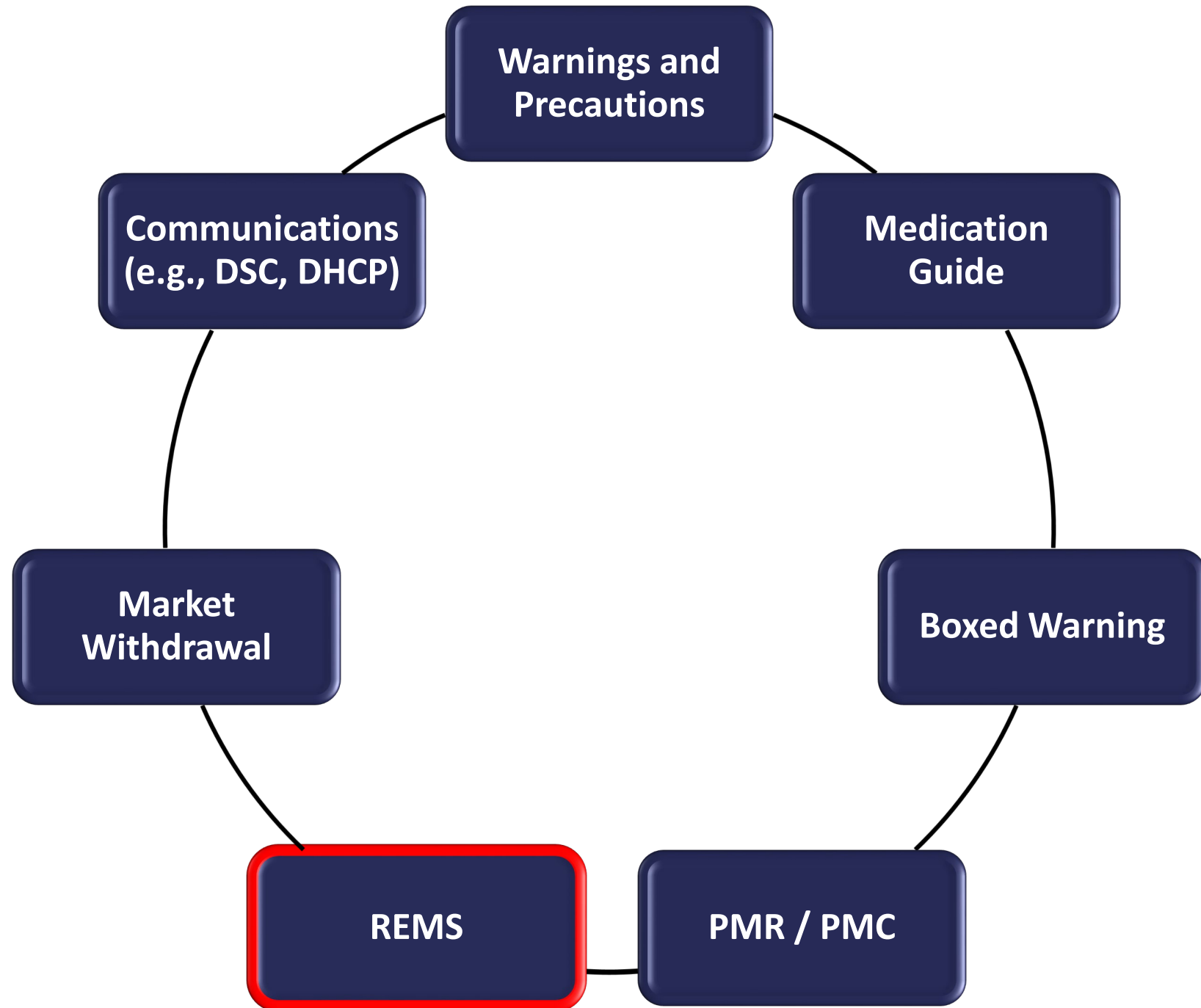




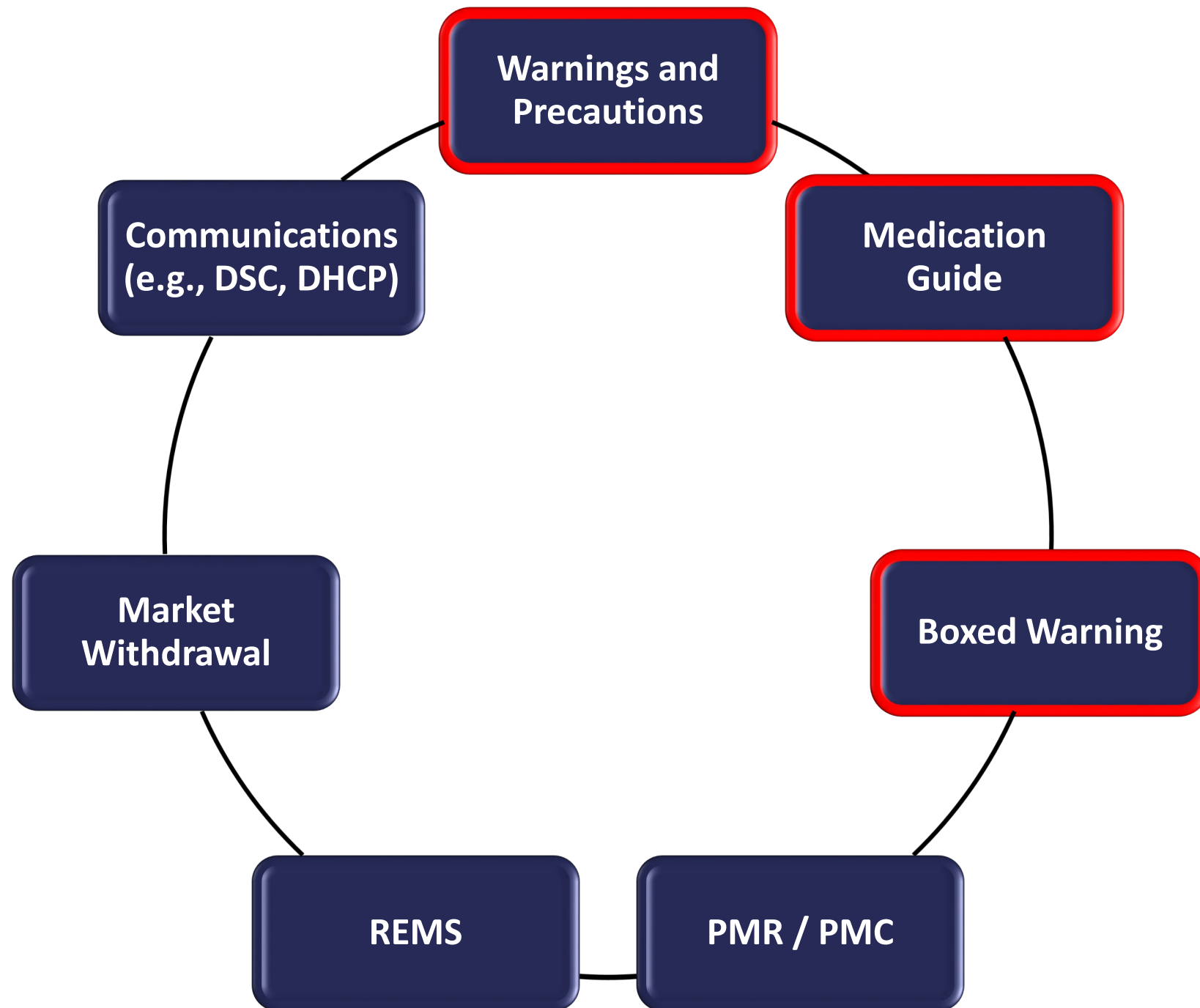












Warnings and Precautions

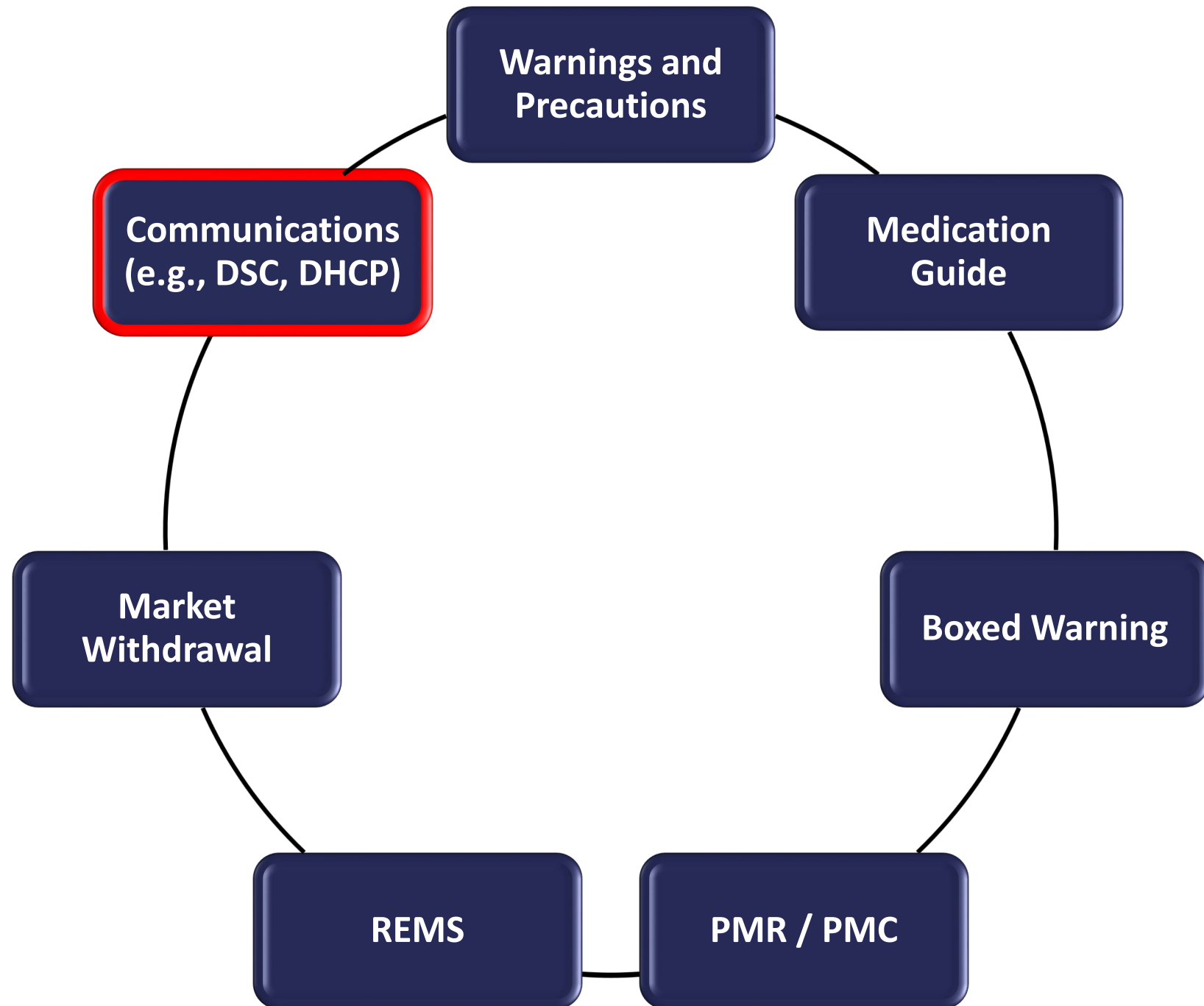
- Describes clinically significant adverse reactions or potential safety hazards
- *21 CFR 201.57(c)(6)*
 - *Adverse reactions are serious or otherwise clinically significant and have implications for prescribing decisions or patient management*
 - *Reasonable evidence of causal association*
- Order should reflect relative clinical significance

Medication Guide

- FDA required patient labeling
- *21 CFR 208.1*
 - *Patient labeling could help prevent serious adverse effects*
 - *Serious risks (relative to benefits) of which patients should be made aware because information could affect decision to use the product*
 - *Patient adherence instructions for use is crucial to drug's effectiveness*

Boxed Warning

- Calls attention to serious or life-threatening risks
- *21 CFR 201.57(c)(1)*
 - *Adverse reaction so serious in proportion to benefit that it is essential to consider in assessing risks and benefits of using the drug*
 - *Serious adverse reaction that can be prevented or reduced by appropriate use*
 - *Approved with restrictions to ensure safe use because drug can be safely used only if distribution or use is restricted*

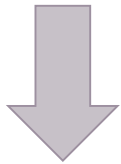


Previous Communication Efforts

- Labeling updates
- Drug Safety Communications
- Dear Health Care Provider letters
- Medscape interview
- Publication in AAP News
- Discussion at open Advisory Committee meetings

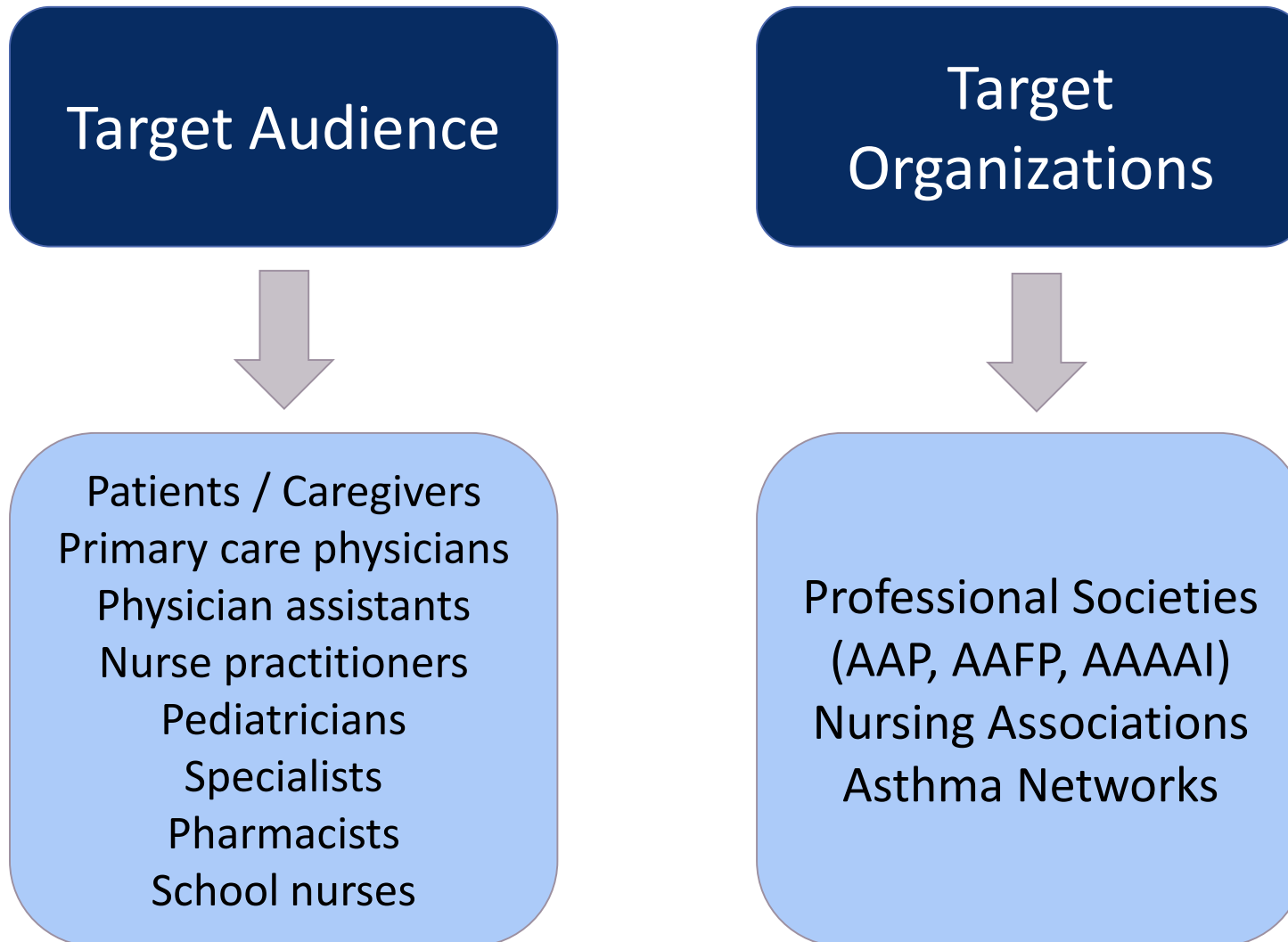
Communication Strategies

Target Audience



Patients / Caregivers
 Primary care physicians
 Physician assistants
 Nurse practitioners
 Pediatricians
 Specialists
 Pharmacists
 School nurses

Communication Strategies



Communication Strategies



Questions for the Committee

1) Discuss the neuropsychiatric safety findings presented for montelukast

Questions for the Committee

2) Discuss the current labeling for montelukast, including:

- *Current Warnings and Precautions*
- *Request for Medication Guide and Boxed Warning*

Questions for the Committee

3) Discuss your recommendations for communication strategies

- *Target audience*
- *Target organizations*
- *Modalities of communication*

